

Refine Search

Search Results -

Terms	Documents
L9 and protein	9

Database:

US Pre-Grant Publication Full-Text Database
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 US OCR Full-Text Database
 EPO Abstracts Database
 JPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Search:

L11

Refine Search

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 DATE: Wednesday, January 07, 2004 [Printable Copy](#) [Create Case](#)

 Set Name Query
 side by side

 Hit Count Set Name
 result set

DB=USPT; PLUR=YES; OP=AND

<u>L11</u>	L9 and protein	9	<u>L11</u>
<u>L10</u>	L9 and pseudomonas	2	<u>L10</u>
<u>L9</u>	las adj a	164	<u>L9</u>
<u>L8</u>	las-a	0	<u>L8</u>
<u>L7</u>	L6 and syndecan	2	<u>L7</u>
<u>L6</u>	L5 and bacteria	297	<u>L6</u>
<u>L5</u>	hydroxamate	1090	<u>L5</u>
<u>L4</u>	tryphostin adj a47	1	<u>L4</u>
<u>L3</u>	tryphostin adj a25	1	<u>L3</u>
<u>L2</u>	tryphostin adj 25	0	<u>L2</u>
<u>L1</u>	syndecan-1	32	<u>L1</u>

END OF SEARCH HISTORY

? save temp

Temp SearchSave "TD280" stored

? rf

Your last SELECT statement was:

S SYNDECAN (2W) SHEDDING

Ref	Items	File
N1	13	34: SciSearch(R) Cited Ref Sci_1990-2003/Dec W4
N2	12	5: Biosis Previews(R)_1969-2003/Dec W4
N3	11	440: Current Contents Search(R)_1990-2004/Jan 01
N4	9	73: EMBASE_1974-2004/Dec W4
N5	9	155: MEDLINE(R)_1966-2004/Jan W1
N6	8	71: ELSEVIER BIOBASE_1994-2004/Jan W1
N7	6	399: CA SEARCH(R)_1967-2003/UD=13926
N8	3	98: General Sci Abs/Full-Text_1984-2003/Nov
N9	3	156: ToxFile_1965-2003/Nov W2
N10	2	143: Biol. & Agric. Index_1983-2003/Nov

21 files have one or more items; file list includes 281 files.

- Enter P or PAGE for more -

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S SYNDECAN (2W) SHEDDING

Ref	Items	File
N11	2	144: Pascal_1973-2003/Dec W2
N12	2	266: FEDRIP_2003/Nov
N13	2	484: Periodical Abs Plustext_1986-2004/Dec W3
N14	1	8: Ei Compendex(R)_1970-2004/Dec W4
N15	1	35: Dissertation Abs Online_1861-2003/Nov
N16	1	65: Inside Conferences_1993-2004/Jan W1
N17	1	148: Gale Group Trade & Industry DB_1976-2004/Jan 06
N18	1	149: TGG Health&Wellness DB(SM)_1976-2004/Dec W2
N19	1	172: EMBASE Alert_2004/Jan W1
N20	1	342: Derwent Patents Citation Indx_1978-01/200370

21 files have one or more items; file list includes 281 files.

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S SYNDECAN (2W) SHEDDING

Ref	Items	File
N21	1	349: PCT FULLTEXT_1979-2002/UB=20031225,UT=20031218
N22	0	2: INSPEC_1969-2003/Dec W2
N23	0	6: NTIS_1964-2004/Jan W1
N24	0	9: Business & Industry(R)_Jul/1994-2003/Dec 29
N25	0	10: AGRICOLA_70-2003/Nov
N26	0	15: ABI/Inform(R)_1971-2004/Jan 06
N27	0	16: Gale Group PROMT(R)_1990-2004/Jan 06
N28	0	18: Gale Group F&S Index(R)_1988-2004/Jan 06
N29	0	19: Chem.Industry Notes_1974-2003/ISS 200352
N30	0	20: Dialog Global Reporter_1997-2004/Jan 06

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? b n1-n21

06jan04 15:41:58 User228210 Session D355.3

\$2.82 1.410 DialUnits File411

\$2.82 Estimated cost File411

\$0.46 TELNET

\$3.28 Estimated cost this search

\$3.29 Estimated total session cost 1.638 DialUnits

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*File 73: New prices as of 1-1-04 per information provider request. See ?RATES 73

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*File 71: New prices as of 1-1-04 per information provider request. See ?RATES 71

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File 149: TGG Health&Wellness DB(SM) 1976-2004/Dec W2

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File 172: EMBASE Alert 2004/Jan W1

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*File 172: New prices as of 1-1-04 per information provider request. See ? RATES 172

File 342: Derwent Patents Citation Indx 1978-01/200370

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*File 342: New prices as of 1/1/04 per Information Provider request. See HELP RATES 342

File 349: PCT FULLTEXT 1979-2002/UB=20031225, UT=20031218

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Set	Items	Description
? s	syndecan (2w)	shedding
	6948	SYNDECAN
	77087	SHEDDING
S1	90	SYNDECAN (2W) SHEDDING

? rd

>>>Duplicate detection is not supported for File 342.

>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.

>>>Record 440:12647650 ignored; incomplete bibliographic data, not retained in RD set

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...examined 50 records (50)

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S2 25 RD (unique items)

? t s2/3,ab/1-25

>>>No matching display code(s) found in file(s): 65, 342

2/3,AB/1 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

12289937 Genuine Article#: 735WU Number of References: 0

Title: Regulation of tissue injury and inflammation by **syndecan-1** ectodomain **shedding**

Author(s): Park PW; Parks WC; Corry DB; Kheradmand F; Duncan S

Corporate Source: Baylor Coll Med, Dept Med, Houston//TX/77030; Washington

Univ, Sch Med, Dept Pediatr, St Louis//MO/63110

Journal: GLYCOBIOLOGY, (2003, V13, N11 (NOV), P830-831

ISSN: 0959-6658 Publication date: 20031100

Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513 USA

Language: English Document Type: MEETING ABSTRACT

2/3,AB/2 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2003 Inst for Sci Info. All rts. reserv.

12129371 Genuine Article#: 730TX Number of References: 60

Title: Cleavage of syndecan-1 by membrane type matrix metalloproteinase-1 stimulates cell migration (ABSTRACT AVAILABLE)

Author(s): Endo K; Takino T; Miyamori H; Kinsen H; Yoshizaki T; Furukawa M; Sato H (REPRINT)

Corporate Source: Kanazawa Univ, Dept Mol Oncol & Virol, 13-1 Takara

Machi/Kanazawa/Ishikawa 9200934/Japan/ (REPRINT); Kanazawa Univ, Dept

Mol Oncol & Virol, Kanazawa/Ishikawa 9200934/Japan/; Kanazawa Univ, Canc

Res Inst, Ctr Dev Mol Target Drugs, Kanazawa/Ishikawa 9200934/Japan/;

Kanazawa Univ, Grad Sch Med Sci, Dept Otolaryngol, Kanazawa/Ishikawa

9200934/Japan/

Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 2003, V278, N42 (OCT 17), P 40764-40770

ISSN: 0021-9258 Publication date: 20031017

Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA

Language: English Document Type: ARTICLE

Abstract: The transmembrane heparan sulfate proteoglycan syndecan-1 was identified from a human placenta cDNA library by the expression cloning method as a gene product that interacts with membrane type matrix metalloproteinase-1 (MT1-MMP). Co-expression of MT1-MMP with syndecan-1 in HEK293T cells promoted **syndecan-1 shedding**, and concentration of cell-associated syndecan-1 was reduced. Treatment of cells with MMP inhibitor BB-94 or tissue inhibitor of MMP (TIMP)-2 but not TIMP-1 interfered with the **syndecan-1 shedding** promoted by MT1-MMP expression. In contrast, **syndecan-1 shedding** induced by 12-O-tetradecanoylphorbol-13-acetate treatment was inhibited by BB-94 but not by either TIMP-1 or TIMP-2. Shedding of syndecan-1 was also induced by MT3-MMP but not by other MT-MMPs. Recombinant syndecan-1 core protein was shown to be cleaved by recombinant MT1-MMP or MT3-MMP preferentially at the Gly(245)-Leu(246) peptide bond. HT1080 fibrosarcoma cells stably transfected with the syndecan-1 cDNA (HT1080/SDC), which express endogenous MT1-MMP, spontaneously shed syndecan-1. Migration of HT1080/ SDC cells on collagen-coated dishes

was significantly slower than that of control HT1080 cells. Treatment of HT1080/ SDC cells with BB-94 or TIMP-2 induced accumulation of syndecan-1 on the cell surface, concomitant with further retardation of cell migration. Substitution of Gly(245) of syndecan-1 with Leu significantly reduced shedding from HT1080/ SDC cells and cell migration. These results suggest that the shedding of syndecan-1 promoted by MT1-MMP through the preferential cleavage of Gly(245)-Leu(246) peptide bond stimulates cell migration.

2/3,AB/3 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

11998258 Genuine Article#: 719RL Number of References: 37
Title: Matrix metalloproteinase-dependent shedding of syndecan-3, a transmembrane heparan sulfate proteoglycan, in Schwann cells (ABSTRACT AVAILABLE)
Author(s): Asundi VK; Erdman R; Stahl RC; Carey DJ (REPRINT)
Corporate Source: Weis Ctr Res, Geisinger Clin, 100 N Acad Ave/Danville//PA/17822 (REPRINT); Weis Ctr Res, Geisinger Clin, Danville//PA/17822
Journal: JOURNAL OF NEUROSCIENCE RESEARCH, 2003, V73, N5 (SEP 1), P593-602
ISSN: 0360-4012 Publication date: 20030901
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS-INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA

Language: English Document Type: ARTICLE

Abstract: Schwann cells transiently express the transmembrane heparan sulfate proteoglycan syndecan-3 during the late embryonic and early postnatal periods of peripheral nerve development. Neonatal rat Schwann cells released soluble syndecan-3 into the culture medium by a process that was blocked by inhibition of endogenous matrix metalloproteinase activity. When Schwann cells were plated on a substratum that binds syndecan-3, the released proteoglycan bound to the substratum adjacent to the cell border. Membrane-anchored syndecan-3 was concentrated in actin-containing filopodia that projected from the lateral edges of the Schwann cell membrane. Membrane shedding was specific for syndecan-3 and was not observed for the related proteoglycan syndecan-1. Analysis of Schwann cells transfected with wild-type and chimeric syndecan-1 and syndecan-3 cDNAs revealed that membrane shedding was a property of the syndecan-3 ectodomain. Inhibition of syndecan-3 release significantly enhanced Schwann cell adhesion and process extension on dishes coated with the non-collagenous N-terminal domain of alpha4(V) collagen, which binds syndecan-3 and mediates heparan sulfate-dependent Schwann cell adhesion. Matrix metalloproteinase-dependent **syndecan-3 shedding** was also observed in newborn rat peripheral nerve tissue. **Syndecan-3 shedding** in peripheral nerve tissue was age specific, and was not observed during later stages of postnatal nerve development. These results demonstrate that Schwann cell syndecan-3 is subject to matrix metalloproteinase-dependent membrane processing, which modulates the biological function of this proteoglycan. (C) 2003 Wiley-Liss, Inc.

2/3,AB/4 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

11933214 Genuine Article#: 710EG Number of References: 50
Title: Plasminogen activator inhibitor-1 supports IL-8-mediated neutrophil transendothelial migration by inhibition of the constitutive shedding of endothelial IL-8/heparan sulfate/syndecan-1 complexes (ABSTRACT AVAILABLE)
Author(s): Marshall LJ; Ramdin LSP; Brooks T; DPhil PC; Shute JK (REPRINT)
Corporate Source: Univ Portsmouth, Sch Pharm & Biomed Sci, St Michaels Bldg, White Swan Rd/Portsmouth PO1 2DT/Hants/England/ (REPRINT); Univ Portsmouth, Sch Pharm & Biomed Sci, Portsmouth PO1 2DT/Hants/England/; Southampton Gen Hosp, Dept Med Specialties, Southampton/Hants/England/;

Xenova Grp Plc, Slough/Berks/England/
Journal: JOURNAL OF IMMUNOLOGY, 2003, V171, N4 (AUG 15), P2057-2065
ISSN: 0022-1767 Publication date: 20030815
Publisher: AMER ASSOC IMMUNOLOGISTS 9650 ROCKVILLE PIKE, BETHESDA, MD
20814 USA

Language: English Document Type: ARTICLE

Abstract: The endothelium is the primary barrier to leukocyte recruitment at sites of inflammation. Neutrophil recruitment is directed by transendothelial gradients of IL-8 that, in vivo, are bound to the endothelial cell surface. We have investigated the identity and function of the binding site(s) in an in vitro model of neutrophil transendothelial migration. In endothelial culture supernatants, IL-8 was detected in a trimolecular complex with heparan sulfate and **syndecan-1**. Constitutive **shedding** of IL-8 in this form was increased in the presence of a neutralizing Ab to plasminogen activator inhibitor-1 (PAI-1), indicating a role for endothelial plasminogen activator in the shedding of IL-8. Increased shedding of IL-8/heparan sulfate/syndecan-1 complexes was accompanied by inhibition of neutrophil transendothelial migration, and aprotinin, a potent plasmin inhibitor, reversed this inhibition. Platelets, added as an exogenous source of PAI-1, had no effect on shedding of the complexes or neutrophil migration. Our results indicate that IL-8 is immobilized on the endothelial cell surface through binding to syndecan-1 ectodomains, and that plasmin, generated by endothelial plasminogen activator, induces the shedding of this form of IL-8. PAI-1 appears to stabilize the chemoattractant form of IL-8 at the cell surface and may represent a therapeutic target for novel anti-inflammatory strategies.

2/3,AB/5 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

11863037 Genuine Article#: 645LF Number of References: 0
Title: **Syndecan-1 shedding** is increased in hemorrhagic shock
and partitions with pro-inflammatory cytokines in blood and body fluids
Author(s): Arikan AA; Yu B; Tweardy DJ
Corporate Source: Baylor Coll Med, Houston//TX/77030
Journal: CRITICAL CARE MEDICINE, 2003, V31, N2, S (FEB), PA41-A41
ISSN: 0090-3493 Publication date: 20030200
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA
19106-3621 USA
Language: English Document Type: MEETING ABSTRACT

2/3,AB/6 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

10106098 Genuine Article#: 480JG Number of References: 0
Title: Microbial pathogens exploit **syndecan shedding** to enhance
their virulence
Author(s): Park PW; Chakraborty A; Duncan SJ; Pier GB; Bernfield M
Corporate Source: Baylor Coll Med, Dept Med, Infect Dis
Sect, Houston//TX/77030; Harvard Univ, Brigham & Womens Hosp, Dept Med,
Channing Lab, Boston//MA/02115; Harvard Univ, Sch Med, Childrens Hosp,
Dept Pediat, Div Newborn Med, Boston//MA/02115
Journal: GLYCOBIOLOGY, 2001, V11, N10 (OCT), P876-877
ISSN: 0959-6658 Publication date: 20011000
Publisher: OXFORD UNIV PRESS INC, JOURNALS DEPT, 2001 EVANS RD, CARY, NC
27513 USA
Language: English Document Type: MEETING ABSTRACT

2/3,AB/7 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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09918850 Genuine Article#: 465CB Number of References: 35

Title: Evidence of a role for a non-matrix-type metalloproteinase activity in the shedding of syndecan-1 from human myeloma cells (ABSTRACT AVAILABLE)

Author(s): Holen I; Drury NL; Hargreaves PG; Croucher PI (REPRINT)
Corporate Source: Univ Sheffield, Sch Med, Div Genom Med, Beech Hill Rd/Sheffield S10 2RX/S Yorkshire/England/ (REPRINT); Univ Sheffield, Sch Med, Div Genom Med, Sheffield S10 2RX/S Yorkshire/England/
Journal: BRITISH JOURNAL OF HAEMATOLOGY, 2001, V114, N2 (AUG), P414-421
ISSN: 0007-1048 Publication date: 20010800
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE, OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Syndecan-1 is a cell surface proteoglycan that is expressed on human myeloma cells and is thought to act as a co-receptor for certain extracellular matrix proteins and growth factors. The ectodomain of syndecan-1 is thought to be shed from the surface of myeloma cells, although the exact mechanism of release remains unclear. In this study, we used a panel of inhibitors to identify the class of proteinase responsible for shedding the soluble syndecan-1 ectodomain from human myeloma cells. Using enzyme-linked immunosorbent assay, flow cytometry and immunocytochemistry, we demonstrated that myeloma cell lines expressed syndecan-1 on their surface and that this was shed constitutively, but to a varying extent. In addition, phorbol 12-myristate 13-acetate (PMA), an activator of protein kinase C, stimulated a marked loss of cell surface syndecan-1 from each of the cell lines and this was associated with a corresponding increase in soluble syndecan-1. Inhibitors of serine and cysteine proteinases, and matrix-type metalloproteinases, did not inhibit constitutive or IMA-stimulated **syndecan-1 shedding** from JJN3 and RPMI 8226 cells. However, BB-94, a hydroxamate-based, broad-spectrum, metalloproteinase inhibitor, substantially suppressed constitutive and PMA-stimulated syndecan-1 loss from myeloma cells. These data indicate that a non-matrix-type metalloproteinase is responsible for **syndecan-1 shedding** from the surface of myeloma cells.

2/3,AB/8 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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09605358 Genuine Article#: 427XY Number of References: 29

Title: Exploitation of **syndecan-1 shedding** by Pseudomonas aeruginosa enhances virulence (ABSTRACT AVAILABLE)

Author(s): Park PW; Pier GB; Hinkes MT; Bernfield M (REPRINT)

Corporate Source: Childrens Hosp, Dept Pediat, Div Newborn Med, Boston//MA/02115 (REPRINT); Childrens Hosp, Dept Pediat, Div Newborn Med, Boston//MA/02115; Harvard Univ, Brigham & Womens Hosp, Sch Med, Dept Med, Channing Lab, Boston//MA/02115

Journal: NATURE, (2001, V411, N6833 (MAY 3), P98-102

ISSN: 0028-0836 Publication date: 20010503

Publisher: MACMILLAN PUBLISHERS LTD, PORTERS SOUTH, 4 CRINAN ST, LONDON N1 9XW, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Cell-surface heparan sulphate proteoglycans (HSPGs) are ubiquitous and abundant receptors/co-receptors of extracellular ligands(1,2), including many microbes(3-10). Their role in microbial infections is poorly defined, however, because no cell-surface HSPG has been clearly connected to the pathogenesis of a particular microbe. We have previously shown that Pseudomonas aeruginosa, through its virulence factor LasA, enhances the in vitro shedding of syndecan-1-the predominant cell-surface HSPG of epithelia(11). Here we show that shedding of syndecan-1 is also activated by P. aeruginosa in vivo, and that the resulting syndecan-1 ectodomains enhance bacterial virulence in newborn mice. Newborn mice deficient in syndecan-1 resist P. aeruginosa lung infection but become susceptible when given purified syndecan-1 ectodomains or heparin, but not when given ectodomain core protein, indicating that the ectodomain's heparan sulphate chains are the effectors. In wild-type newborn mice, inhibition of **syndecan-1 shedding** or inactivation of the shed ectodomain's heparan

sulphate chains prevents lung infection. Our findings uncover a pathogenetic mechanism in which a host response to tissue injury- **syndecan-1 shedding**-is exploited to enhance microbial virulence apparently by modulating host defences.

2/3,AB/9 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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08454985 Genuine Article#: 287NB Number of References: 86
Title: Shedding of syndecan-1 and-4 ectodomains is regulated by multiple signaling pathways and mediated by a TIMP-3-sensitive metalloproteinase (ABSTRACT AVAILABLE)
Author(s): Fitzgerald ML; Wang ZH; Park PW; Murphy G; Bernfield M (REPRINT)
Corporate Source: HARVARD UNIV,SCH MED, DIV NEWBORN MED, CHILDRENS HOSP, 300 LONGWOOD AVE, ENDERS 9/BOSTON//MA/02115 (REPRINT); HARVARD UNIV,SCH MED, DIV NEWBORN MED, CHILDRENS HOSP/BOSTON//MA/02115; UNIV E ANGLIA,SCH BIOL SCI/NORWICH NR4 7TU/NORFOLK/ENGLAND/
Journal: JOURNAL OF CELL BIOLOGY, 2000, V148, N4 (FEB 21), P811-824
ISSN: 0021-9525 Publication date: 20000221
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021

Language: English Document Type: ARTICLE

Abstract: The syndecan family of four transmembrane heparan sulfate proteoglycans binds a variety of soluble and insoluble extracellular effecters. Syndecan extracellular domains (ectodomains) can be shed intact by proteolytic cleavage of their core proteins, yielding soluble proteoglycans that retain the binding properties of their cell surface precursors. Shedding is accelerated by PMA activation of protein kinase C, and by ligand activation of the thrombin (G-protein-coupled) and EGF (protein tyrosine kinase) receptors (Subramanian, S.V., M.L. Fitzgerald, and M. Bernfield. 1997, J. Biol. Chem. 272:14713-14720). Syndecan-1 and -4 ectodomains are found in acute dermal wound fluids, where they regulate growth factor activity (Kato, M., H. Wang, V. Kainulainen, M.L. Fitzgerald, S. Ledbetter, D.M. Ornitz, and M. Bernfield, 1998, Nat, Men, 4:691-697) and proteolytic balance (Kainulainen, V., H. Wang, C. Schick, and M. Bernfield. 1998, J, Biol. Chem, 273: 11563-11569). However, little is known about how **syndecan** ectodomain **shedding** is regulated.

To elucidate the mechanisms that regulate **syndecan** **shedding**, we analyzed several features of the process that sheds the syndecan-1 and -4 ectodomains. We find that shedding accelerated by various physiologic agents involves activation of distinct intracellular signaling pathways; and the proteolytic activity responsible for cleavage of syndecan core proteins, which is associated with the cell surface, can act on unstimulated adjacent cells, and is specifically inhibited by TIMP-3, a matrix-associated metalloproteinase inhibitor. In addition, we find that the syndecan-1 core protein is cleaved on the cell surface at a juxtamembrane site; and the proteolytic activity responsible for accelerated shedding differs from that involved in constitutive shedding of the syndecan ectodomains. These results demonstrate the existence of highly regulated mechanisms that can rapidly convert syndecans from cell surface receptors or coreceptors to soluble heparan sulfate proteoglycan effecters. Because the shed ectodomains are found and function in vivo, regulation of **syndecan** ectodomain **shedding** by physiological mediators indicates that shedding is a response to specific developmental and pathophysiological cues.

2/3,AB/10 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

08397569 Genuine Article#: 281FD Number of References: 59
Title: **Syndecan-1 shedding** is enhanced by LasA, a secreted

virulence factor of *Pseudomonas aeruginosa* (ABSTRACT AVAILABLE)
Author(s): Park PW; Pier GB; Preston MJ; Goldberger O; Fitzgerald ML;
Bernfield M (REPRINT)
Corporate Source: HARVARD UNIV, CHILDRENS HOSP, SCH MED, DEPT MED, DIV
NEWBORN MED, 300 LONGWOOD AVE, ENDER/BOSTON//MA/02115 (REPRINT);
HARVARD UNIV, CHILDRENS HOSP, SCH MED, DEPT MED, DIV NEWBORN
MED/BOSTON//MA/02115; HARVARD UNIV, BRIGHAM & WOMENS HOSP, SCH MED, DEPT
MED, CHANNING LAB/BOSTON//MA/02115
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 2000, V275, N5 (FEB 4), P
3057-3064
ISSN: 0021-9258 Publication date: 20000204
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE
PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE

Abstract: Microbial pathogens frequently take advantage of host systems for their pathogenesis. Shedding of cell surface molecules as soluble extracellular domains (ectodomains) is one of the host responses activated during tissue injury. In this study, we examined whether pathogenic bacteria can modulate shedding of syndecan-1, the predominant syndecan of host epithelia. Our studies found that overnight culture supernatants of *Pseudomonas aeruginosa* and *Staphylococcus aureus* enhanced the shedding of syndecan-1 ectodomains, whereas culture supernatants of several other Gram-negative and Gram-positive bacteria had only low levels of activity. Because supernatants from all tested strains of *P. aeruginosa* (n = 9) enhanced **syndecan-1 shedding** by more than 4-fold above control levels, we focused our attention on this Gram-negative bacterium. Culture supernatants of *P. aeruginosa* increased shedding of syndecan-1 in both a concentration- and time-dependent manner, and augmented shedding by various host cells. A 20-kDa shedding enhancer was partially purified from the supernatant through ammonium sulfate precipitation and gel chromatography, and identified by N-terminal sequencing as LasA, a known *P. aeruginosa* virulence factor. LasA was subsequently determined to be a **syndecan-1 shedding** enhancer from the findings that (i) immunodepletion of LasA from the partially purified sample resulted in abrogation of its activity to enhance shedding and (ii) purified LasA increased shedding in a concentration-dependent manner. Our results also indicated that LasA enhances **syndecan-1 shedding** by activation of the host cell's shedding mechanism and not by direct interaction with syndecan-1 ectodomains. Enhanced **syndecan-1 shedding** may be a means by which pathogenic bacteria take advantage of a host mechanism to promote their pathogenesis.

2/3, AB/11 (Item 11 from file: 34)
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

05858761 Genuine Article#: XC327 Number of References: 69
Title: Regulated shedding of syndecan-1 and -4 ectodomains by thrombin and growth factor receptor activation (ABSTRACT AVAILABLE)
Author(s): Subramanian SV; Fitzgerald ML; Bernfield M (REPRINT)
Corporate Source: HARVARD UNIV, SCH MED, JOINT PROGRAM NEONATOL, 300
LONGWOOD AVE/BOSTON//MA/02115 (REPRINT); HARVARD UNIV, SCH MED, JOINT
PROGRAM NEONATOL/BOSTON//MA/02115
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1997, V272, N23 (JUN 6), P
14713-14720
ISSN: 0021-9258 Publication date: 19970606
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE
PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE

Abstract: The syndecan family of transmembrane heparan sulfate proteoglycans is abundant on the surface of all adherent mammalian cells. Syndecans bind and modify the action of various growth factors/cytokines, proteases/antiproteases, cell adhesion molecules, and extracellular matrix components. Syndecan expression is highly regulated during wound repair, a process orchestrated by many of these effectors. Each syndecan ectodomain is shed constitutively by cultured

cells, but the mechanism and significance of this shedding are not understood. Therefore, we examined (i) whether physiological agents active during wound repair influence **syndecan shedding**, and (ii) whether wound fluids contain shed syndecan ectodomains.

Using SVEC4-10 endothelial cells we find that certain proteases and growth factors accelerate shedding of the syndecan-1 and -4 ectodomains. Protease-accelerated shedding is completely inhibited by serum-containing media. Thrombin activity is duplicated by the 14-amino acid thrombin receptor agonist peptide that directly activates the thrombin receptor and is not inhibited by serum. Epidermal growth factor family members accelerate shedding but FGF-S, platelet-derived growth factor-AB, transforming growth factor-beta, tumor necrosis factor-cu, and vascular endothelial cell growth factor 165 do not. Shed ectodomains are soluble, stable in the conditioned medium, have the same size core proteins regardless whether shed at a basal rate, or accelerated by thrombin or epidermal growth factor-family members and are found in acute human dermal wound fluids. Thus, shedding is accelerated by activation of at least two distinct receptor classes, Gr protein-coupled (thrombin) and protein tyrosine kinase (epidermal growth factor). Proteases and growth factors active during wound repair can accelerate **syndecan shedding** from cell surfaces. Regulated shedding of syndecans suggests physiological roles for the soluble proteoglycan ectodomains.

2/3,AB/12 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2003 Inst for Sci Info. All rts. reserv.

01578888 Genuine Article#: HK318 Number of References: 66
Title: GROWTH-FACTORS INDUCE 3T3 CELLS TO EXPRESS BFGF-BINDING SYNDECAN (Abstract Available)
Author(s): ELENIOUS K; MAATTA A; SALMIVIRTA M; JALKANEN M
Corporate Source: UNIV TURKU,DEPT MED BIOCHEM,KIINAMYLLENKATU 10/SF-20520
TURKU 52//FINLAND/; UNIV TURKU,DEPT MED BIOCHEM,KIINAMYLLENKATU
10/SF-20520 TURKU 52//FINLAND/; TURKU BIOTECHNOL CTR/SF-20521
TURKU//FINLAND/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1992, V267, N9 (MAR 25), P
6435-6441

Language: ENGLISH Document Type: ARTICLE

Abstract: Syndecan is an integral membrane proteoglycan that putatively binds extracellular matrix molecules and growth factors at the surfaces of several cell types. Syndecan is also transiently expressed in several condensing mesenchymes after epithelial induction. In order to understand the mechanism(s) that regulate(s) syndecan expression in early mesenchymal cells, we have studied the effects of growth factors on the expression of syndecan in 3T3 fibroblasts and compared these results to NMuMG epithelial cells. Our studies indicate that (i) two developmentally important growth factors, basic fibroblast growth factor (bFGF) and transforming growth factor beta(TGF-beta), especially when administrated at the same time, increase syndecan expression in 3T3 cells both at the mRNA and protein level. (ii) Furthermore, the same growth factors also increase **syndecan shedding** into the culture medium of 3T3 cells. No such stimulation of **syndecan** synthesis or **shedding** was observed with NMuMG cells. (iii) Syndecan isolated from the cell surface of bFGF + TGF-beta-treated 3T3 cells binds bFGF. (iv) Induced expression of syndecan correlates with enhanced binding of bFGF to the cell surface of 3T3 cells, and (v) this interaction can be inhibited by exogenous ectodomain of syndecan. These results suggest a key role for growth factors in the regulation of syndecan expression during organogenesis and, moreover, an involvement of syndecan in the regulation of growth factor action.

2/3,AB/13 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0011227464 BIOSIS NO.: 199800021711

Shedding of syndecan ectodomains is regulated by multiple pathways and metalloproteinase-dependent

AUTHOR: Fitzgerald M L; Bernfield M

AUTHOR ADDRESS: Program Biological Biomedical Sci., Harvard Med. Sch., Boston, MA 02115, USA**USA

JOURNAL: Molecular Biology of the Cell 8 (SUPPL.): p393A Nov., 1997 1997

MEDIUM: print

CONFERENCE/MEETING: 37th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 13-17, 1997; 19971213

SPONSOR: American Society for Cell Biology

ISSN: 1059-1524

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Citation

LANGUAGE: English

2/3,AB/14 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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10591741 EMBASE No: 2000056980

Syndecan-1 shedding is enhanced by LasA, a secreted virulence factor of *Pseudomonas aeruginosa*

Pyong Woo Park; Pier G.B.; Preston M.J.; Goldberger O.; Fitzgerald M.L.; Bernfield M.

M. Bernfield, Children's Hospital, Harvard Medical School, Enders-9, 300 Longwood Ave., Boston, MA 02115 United States

AUTHOR EMAIL: bernfield@al.tch.harvard.edu

Journal of Biological Chemistry (J. BIOL. CHEM.) (United States) 04 FEB 2000, 275/5 (3057-3064)

CODENT: JBCHA ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 59

Microbial pathogens frequently take advantage of host systems for their pathogenesis. Shedding of cell surface molecules as soluble extracellular domains (ectodomains) is one of the host responses activated during tissue injury. In this study, we examined whether pathogenic bacteria can modulate shedding of syndecan-1, the predominant syndecan of host epithelia. Our studies found that overnight culture supernatants of *Pseudomonas aeruginosa* and *Staphylococcus aureus* enhanced the shedding of syndecan-1 ectodomains, whereas culture supernatants of several other Gram-negative and Gram-positive bacteria had only low levels of activity. Because supernatants from all tested strains of *P. aeruginosa* (n = 9) enhanced **syndecan-1 shedding** by more than 4-fold above control levels, we focused our attention on this Gram-negative bacterium. Culture supernatants of *P. aeruginosa* increased shedding of syndecan-1 in both a concentration- and time-dependent manner, and augmented shedding by various host cells. A 20-kDa shedding enhancer was partially purified from the supernatant through ammonium sulfate precipitation and gel chromatography, and identified by N-terminal sequencing as LasA, a known *P. aeruginosa* virulence factor. LasA was subsequently determined to be a **syndecan-1 shedding** enhancer from the findings that (i) immunodepletion of LasA from the partially purified sample resulted in abrogation of its activity to enhance shedding and (ii) purified LasA increased shedding in a concentration-dependent manner. Our results also indicated that LasA enhances **syndecan-1 shedding** by activation of the host cell's shedding mechanism and not by direct interaction with syndecan-1 ectodomains. Enhanced **syndecan-1 shedding** may be a means by which pathogenic bacteria take advantage of a host mechanism to promote their pathogenesis.

2/3,AB/15 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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135088769 CA: 135(7)88769x DISSERTATION
Regulation of syndecan ectodomain shedding
AUTHOR(S): Fitzgerald, Marilyn Lee
LOCATION: Harvard Univ., Cambridge, MA, USA
DATE: 2000 PAGES: 279 pp. CODEN: DABBBB LANGUAGE: English CITATION:
Diss. Abstr. Int., B 2000, 61(5), 2319 AVAIL: UMI, Order No. DA9972310

2/3,AB/16 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

134217179 CA: 134(16)217179k PATENT
Method based on syndecan-1 shedding inhibition for treating and
preventing bacterial infection
INVENTOR(AUTHOR): Bernfield, Merton; Park, Pyong Woo
LOCATION: USA
ASSIGNEE: Children's Medical Center Corp.
PATENT: PCT International ; WO 200117560 A1 DATE: 20010315
APPLICATION: WO 2000US24839 (20000911) *US PV153310 (19990910)
PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A;
A61K-039/02B; A61K-039/085B; A61K-039/108B; C12Q-001/00B; C12Q-001/18B;
C07K-001/00B; C07K-016/00B DESIGNATED COUNTRIES: AU; CA; JP; US
DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT;
LU; MC; NL; PT; SE

2/3,AB/17 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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04045913 H.W. WILSON RECORD NUMBER: BGS199045913
Functions of cell surface heparan sulfate proteoglycans.
Bernfield, Merton
Gotte, Martin; Park, Pyong Woo
Annual Review of Biochemistry v. 68 (1999) p. 729-77
SPECIAL FEATURES: bibl il ISSN: 0066-4154
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 19594

ABSTRACT: The heparan sulfate on the surface of all adherent cells
modulates the actions of a large number of extracellular ligands. Members
of both cell surface heparan sulfate proteoglycan families, the
transmembrane syndecans and the glycosylphosphoinositide-linked glypicans,
bind these ligands and enhance formation of their receptor-signaling
complexes. These heparan sulfate proteoglycans also immobilize and regulate
the turnover of ligands that act at the cell surface. The extracellular
domains of these proteoglycans can be shed from the cell surface,
generating soluble heparan sulfate proteoglycans that can inhibit
interactions at the cell surface. Recent analyses of genetic defects in
Drosophila melanogaster, mice, and humans confirm most of these activities
in vivo and identify additional processes that involve cell surface heparan
sulfate proteoglycans. This chapter focuses on the mechanisms underlying
these activities and on the cellular functions that they regulate.
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2/3,AB/18 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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15084459 PASCAL No.: 01-0244069
Exploitation of **syndecan-1 shedding** by Pseudomonas aeruginosa
enhances virulence
PYENG WOO PARK; PLER Gerald B; HINKES Michael T; BERNFLELD Merton
Division of Newborn Medicine, Department of Pediatrics, Children's
Hospital, Harvard Medical School, Boston, Massachusetts 02115, United
States; Channing Laboratory, Department of Medicine, Brigham and Women's

Hospital, Harvard Medical School, Boston, Massachusetts 02115, United States

Journal: Nature : (London) 2001, 411 (6833) 98-102

Language: English

Cell-surface heparan sulphate proteoglycans (HSPGs) are ubiquitous and abundant receptors/co-receptors of extracellular ligands SUP 1 SUP , SUP 2 , including many microbes SUP 3 SUP - SUP 1 SUP 0 . Their role in microbial infections is poorly defined, however, because no cell-surface HSPG has been clearly connected to the pathogenesis of a particular microbe. We have previously shown that *Pseudomonas aeruginosa*, through its virulence factor LasA, enhances the in vitro shedding of syndecan-1-the predominant cell-surface HSPG of epithelia SUP 1 SUP 1 . Here we show that shedding of syndecan-1 is also activated by *P. aeruginosa* in vivo, and that the resulting syndecan-1 ectodomains enhance bacterial virulence in newborn mice. Newborn mice deficient in syndecan-1 resist *P. aeruginosa* lung infection but become susceptible when given purified syndecan-1 ectodomains or heparin, but not when given ectodomain core protein, indicating that the ectodomain's heparan sulphate chains are the effectors. In wild-type newborn mice, inhibition of syndecan-1 shedding or inactivation of the shed ectodomain's heparan sulphate chains prevents lung infection. Our findings uncover a pathogenetic mechanism in which a host response to tissue injury-syndecan-1 shedding-is exploited to enhance microbial virulence apparently by modulating host defences.

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2/3,AB/19 (Item 1 from file: 266)

DIALOG(R)File 266:FEDRIP

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00353946

IDENTIFYING NO.: 5R01HL69050-02 AGENCY CODE: CRISP

Proteoglycans in Microbial Pathogenesis and Host Defense

PRINCIPAL INVESTIGATOR: PARK, PYONG W

ADDRESS: PWPARK@BCM.TMC.EDU BAYLOR COLLEGE OF MEDICINE ONE BAYLOR PL, BCM 286, RM NI319

PERFORMING ORG.: BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

SPONSORING ORG.: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

DATES: 2012/01/01 TO 2011/30/05 FY : 2003

SUMMARY: DESCRIPTION (provided by applicant) Microbial infection is a major public health threat that can be associated with high mortality, and that can also often amplify and lead to chronic inflammation, also resulting in serious complications. The current emergence of multi-drug resistant strains adds to the threat of infections. These features are especially evident in compromised patients in whom drug-resistant microbial pathogens infect with high mortality and morbidity. During infection, microbes exploit a variety of host components to promote their pathogenesis. Among these, cell surface heparan sulfate proteoglycans (HSPGs) are targeted by a wide spectrum of microbes. Cell surface HSPGs function as selective regulators of various molecular interactions, including those important to microbial pathogenesis and host defense. These HSPGs not only function at the cell surface, but also in the extracellular environment as soluble HSPGs because they can be shed as intact ectodomains in response to tissue injury, including those caused by infections. The long term objective of this research is to delineate how cell surface HSPGs regulate, in part, the highly complex host response to microbial infections. This proposal focuses on the role of syndecan-1, the predominant cell surface HSPG of epithelia. The goal of this application is to elucidate the molecular mechanisms that are responsible for exploitation of syndecan-1 shedding by bacterial pathogens to enhance their lung virulence. Three inter-related hypotheses will be tested in three aims: Specific Aim 1. Binding of certain virulence factors to their host receptors triggers signaling events that lead to activation of syndecan-1 shedding will be assessed by determining in molecular detail how LasA, a virulence factor for *Pseudomonas aeruginosa* lung infection, activates syndecan-1 shedding; Specific Aim 2. Syndecan-1 ectodomains regulate the host response by inhibiting innate defense mechanisms will be evaluated by establishing whether syndecan-1

ectodomains, via their specific structural features in their HS chains, inhibit the activity of cytokines and antimicrobials to enhance bacterial virulence in the lung; and Specific Aim 3. This mechanism is used by several major pulmonary bacterial pathogens will be probed by evaluating whether *Staphylococcus aureus* exploits **syndecan-1 shedding** to enhance its lung virulence. These studies, which delineate how cell surface HSPGs such as syndecan-1 are exploited by microbes for their pathogenesis, should provide a foundation for the development of novel prophylactic and therapeutic agents to combat infections caused by major opportunistic bacterial pathogens.

2/3,AB/20 (Item 2 from file: 266)
DIALOG(R)File 266:FEDRIP
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00351752

IDENTIFYING NO.: 2R01HL60903-05 AGENCY CODE: CRISP

Syndecan Shedding in Vascular Lesion Formation

PRINCIPAL INVESTIGATOR: CHAIKOF, ELLIOT L

ADDRESS: ECHAIKO@EMORY.EDU EMORY UNIVERSITY 1639 PIERCE DR, ROOM 5105

PERFORMING ORG.: EMORY UNIVERSITY, ATLANTA, GEORGIA

SPONSORING ORG.: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

DATES: 2007/01/98 TO 2002/28/06 FY: 2003

SUMMARY: DESCRIPTION (provided by applicant): We postulate that oxidized lipids, as well as local mechanical stress regulate the expression and shedding of syndecan-1 and -4 as an initial adaptive response that ultimately contributes to the generation of a sustained proinflammatory, growth-stimulating environment that leads to vascular lesion formation. In particular, we speculate that syndecans shed in response to these pro-inflammatory stimuli will preferentially bind and effectively sequester chemokines and proteases relevant to vascular lesion formation. Specifically, we plan to (1) Determine the capacity of arterial wall mechanics and oxidized lipids, both as isolated and interactive factors, to modulate **syndecan** expression and **shedding**. The expression of syndecan-1 and -4 will be characterized in hypertensive ApoE deficient mice using immunohistochemical and in situ hybridization techniques. Moreover, correlative in vitro studies will be performed to determine the capacity of cyclic mechanical stress and oxidized lipids, both as isolated and interactive factors, to potentiate **syndecan** expression and **shedding** in vascular smooth muscle cells and periadventitial fibroblasts. (2) Characterize the signal transduction pathways activated by mechanical stress and oxidized lipids that converge in regulating **syndecan** expression and **shedding**. The extents to which redox-sensitive and insensitive MAP kinase signaling pathways initiated in response to mechanical stress and oxidized lipids converge in regulating **syndecan shedding** and expression will be determined. Furthermore, the potential that unique pathways differentially regulate **syndecan** expression and **shedding** will be investigated and the role of metalloproteinases as primary mediators of accelerated **syndecan shedding** in vascular mesenchymal cells will be defined. (3) Define the molecular binding interactions between shed syndecans and selected proatherogenic chemokines and proteases. The relative binding affinities of selected chemokines (RANTES, MCP-1) and proteases (MMP-2, MMP-9) to syndecan associated heparan sulfate chains shed in response to oxidized lipids and/or mechanical stress will be characterized and the susceptibility of the complexed protein to degradation will be defined. This data will facilitate subsequent studies directed at assessing the capacity of pharmacological inhibitors of heparan and chondroitin sulfate, as well as **syndecan shedding** to limit the formation of pro-inflammatory or proteolytically active solid phase gradients in vitro and in vivo.

2/3,AB/21 (Item 1 from file: 484)
DIALOG(R)File 484:Periodical Abs Plustext
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05060319 SUPPLIER NUMBER: 73063125

Exploitation of **syndecan-1 shedding** by *Pseudomonas aeruginosa*
enhances virulence
Woo, Pyong; Pier, Gerald B; Hinkes, Michael T; Bernfield, Merton
Nature (GNAA), v411 n6833, p98-102
May 3, 2001
ISSN: 0028-0836 JOURNAL CODE: GNAA
DOCUMENT TYPE: Feature
LANGUAGE: English RECORD TYPE: Abstract

ABSTRACT: Cell-surface heparan sulphate proteoglycans (HSPGs) are ubiquitous and abundant receptors/co-receptors of extracellular ligands, including many microbes. Their role in microbial infections is poorly defined, however, because no cell-surface HSPG has been clearly connected to the pathogenesis of a particular microbe.

2/3,AB/22 (Item 2 from file: 484)
DIALOG(R)File 484:Periodical Abs Plustext
(c) 2004 ProQuest. All rts. reserv.

04370923 (USE FORMAT 7 OR 9 FOR FULLTEXT)
Heparin, cell adhesion, and pathogenesis of inflammatory bowel disease
Day, Richard; Forbes, Alastair
Lancet (GLAN), v354 n9172, p62-65, p.4
Jul 3, 1999
ISSN: 0140-6736 JOURNAL CODE: GLAN
DOCUMENT TYPE: Feature
LANGUAGE: English RECORD TYPE: Fulltext; Abstract
WORD COUNT: 2473

ABSTRACT: Tissue repair involves a close interplay between growth factors and cell adhesion molecules. Day and Forbes suggest that the beneficial response to heparin observed in inflammatory bowel disease may result from mechanisms in addition to anticoagulation.

2/3,AB/23 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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04494518 INSIDE CONFERENCE ITEM ID: CN047012790
Syndecan-1 Shedding is Increased in Hemorrhagic Shock and
Partitions with Pro-Inflammatory Cytokines in Blood and Body Fluids
CONFERENCE: Society of Critical Care Medicine-Critical care congress;
32nd
CRITICAL CARE MEDICINE -BALTIMORE-, 2003; VOL 31; NO 2; SUPPL P: A41
Society of Critical Care Medicine, 2002
ISSN: 0090-3493
LANGUAGE: English DOCUMENT TYPE: Conference Preprinted abstracts
CONFERENCE SPONSOR: Society of Critical Care Medicine
CONFERENCE LOCATION: San Antonio, TX 2003; Jan (200301) (200301)
NOTE:
See same s/m vol 30 no 12 suppl 2003 for more preprinted abstracts

2/3,AB/24 (Item 1 from file: 342)
DIALOG(R)File 342:Derwent Patents Citation Indx
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04468033 WPI Acc No: 01-235165/24
Treating or preventing bacterial (e.g. *Pseudomonas* or *Staphylococcus*)
infections, particularly infections of the lung, urinary tract, skin, eye
or bloodstream, comprises administering a compound that inhibits syndecan-1
shedding -
Patent Assignee: (CHIL-) CHILDRENS MEDICAL CENT
Author (Inventor): BERNFIELD M; PARK P W
Patent (basic)
Patent No Kind Date Examiner Field of Search
WO 200117560 A1 010315 (BASIC)

Derwent Week (Basic): 0124
Priority Data: US 153310P (990910)
Applications: AU 200073670 (000911); WO 2000US24839 (000911)
Designated States
(National): AU; CA; JP; US
(Regional): AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC;
NL; PT; SE
Derwent Class: B04; D16
Int Pat Class: A61K-039/02; A61K-039/085; A61K-039/108; A61K-039/395;
C07K-001/00; C07K-016/00
Number of Patents: 002
Number of Countries: 022
Number of Cited Patents: 000
Number of Cited Literature References: 003
Number of Citing Patents: 000

2/3,AB/25 (Item 1 from file: 349)
DIALOG(R) File 349:PCT FULLTEXT
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00785686

METHOD FOR TREATING AND PREVENTING BACTERIAL INFECTION
PROCEDE DE TRAITEMENT ET DE PREVENTION DES INFECTIONS BACTERIENNES
Patent Applicant/Assignee:

CHILDREN'S MEDICAL CENTER CORPORATION, 300 Longwood Avenue, Boston, MA
02115, US, US (Residence), US (Nationality), (For all designated states
except: US)

Patent Applicant/Inventor:

BERNFELD Merton, 25 Brimmer Street, Boston, MA 02108-1040, US, US
(Residence), US (Nationality), (Designated only for: US)
PARK Pyong Woo, 1277 Commonwealth Avenue, Allston, MA 02134, US, US
(Residence), KR (Nationality), (Designated only for: US)

Legal Representative:

RESNICK David S (et al) (agent), Nixon Peabody LLP, 101 Federal Street,
Boston, MA 02110, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200117560 A1 20010315 (WO 0117560)
Application: WO 2000US24839 20000911 (PCT/WO US0024839)
Priority Application: US 99153310 19990910

Designated States: AU CA JP US

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Filing Language: English

Fulltext Word Count: 12825

English Abstract

The present invention provides methods and compositions for treating bacterial infections, especially infections by opportunistic pathogens in a subject by administering a compound that inhibits **syndecan-1 shedding**. The invention is based on the discovery that two diverse opportunistic pathogens, *S. aureus* and *P. aeruginosa*, enhance **syndecan-1 shedding** and that this shedding is critical for *Pseudomonas* pathogenesis via the respiratory tract. The discovery is also based on the surprising finding that inhibition of **syndecan-1 shedding** prevents *Pseudomonas* pneumonia in a mammalian model. The *P. aeruginosa* shedding enhancer has been purified and identified as the mature 20 kDa LasA protein, a known virulence factor of *P. aeruginosa*.

French Abstract

La presente invention porte sur des procedes et sur des compositions visant a traiter des infections bacteriennes, notamment des infections imputables a des agents pathogenes opportunistes en administrant a un sujet un compose qui inhibe l'elimination de syndecan-1. L'invention repose sur la decouverte de deux agents pathogenes opportunistes differents, *S. aureus* et *P. aeruginosa*, qui facilitent l'elimination de syndecan-1, cette elimination etant critique pour la pathogenese de *Pseudomonas* via les voies respiratoires. Cette decouverte s'est averee egalement surprenante par le fait que l'inhibition de l'elimination de

syndecan-1 previent la pneumonie generee par Pseudomonas chez un modele mammalien. L'activateur de l'elimination de P. aeruginosa a ete purifie et identifie sous forme de la proteine mature 20 kDa LasA, un facteur virulent connu de P. aeruginosa.

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? ss e4-e8, e11, e12

S3 25 AU=BERNFELD, M.
S4 1 AU=BERNFELD, M. R.
S5 139 AU=BERNFELD, MERTON
S6 2 AU=BERNFELD, MERTON R
S7 26 AU=BERNFELD, MERTON R.
S8 1 AU=BERNFELD MERTON
S9 1 AU=BERNFELD, MERTON
S10 195 E4-E8, E11, E12

? rd

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>>>Duplicate detection is not supported for File 349.

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...examined 50 records (50)
...examined 50 records (100)
...examined 50 records (150)
...completed examining records
S11 157 RD (unique items)

? s s11 and syndecan

157 S11
6948 SYNDECAN

S12 53 S11 AND SYNDECAN

? s s12 and bacteria?

53 S12
3596806 BACTERIA?
S13 3 S12 AND BACTERIA?

? t s13/3,ab/1-3

>>>No matching display code(s) found in file(s): 65, 342

13/3,AB/1 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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134217179 CA: 134(16)217179k PATENT

Method based on syndecan-1 shedding inhibition for treating and preventing bacterial infection

INVENTOR(AUTHOR): Bernfield, Merton; Park, Pyong Woo

LOCATION: USA

ASSIGNEE: Children's Medical Center Corp.

PATENT: PCT International ; WO 200117560 A1 DATE: 20010315

APPLICATION: WO 2000US24839 (20000911) *US PV153310 (19990910)

PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A;

A61K-039/02B; A61K-039/085B; A61K-039/108B; C12Q-001/00B; C12Q-001/18B;

C07K-001/00B; C07K-016/00B DESIGNATED COUNTRIES: AU; CA; JP; US

DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

13/3,AB/2 (Item 1 from file: 144)

DIALOG(R)File 144:Pascal

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15084459 PASCAL No.: 01-0244069

Exploitation of **syndecan-1** shedding by *Pseudomonas aeruginosa* enhances virulence

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Journal: Nature : (London), 2001, 411 (6833) 98-102

Language: English

Cell-surface heparan sulphate proteoglycans (HSPGs) are ubiquitous and abundant receptors/co-receptors of extracellular ligands SUP 1 SUP , SUP 2 , including many microbes SUP 3 SUP - SUP 1 SUP 0 . Their role in microbial

not prior

infections is poorly defined, however, because no cell-surface HSPG has been clearly connected to the pathogenesis of a particular microbe. We have previously shown that *Pseudomonas aeruginosa*, through its virulence factor LasA, enhances the in vitro shedding of **syndecan-1**-the predominant cell-surface HSPG of epithelia SUP 1 SUP 1 . Here we show that shedding of **syndecan -1** is also activated by *P. aeruginosa*, in vivo, and that the resulting **syndecan-1** ectodomains enhance **bacterial** virulence in newborn mice. Newborn mice deficient in **syndecan -1** resist *P. aeruginosa* lung infection but become susceptible when given purified **syndecan-1** ectodomains or heparin, but not when given ectodomain core protein, indicating that the ectodomain's heparan sulphate chains are the effectors. In wild-type newborn mice, inhibition of **syndecan-1** shedding or inactivation of the shed ectodomain's heparan sulphate chains prevents lung infection. Our findings uncover a pathogenetic mechanism in which a host response to tissue injury-**syndecan -1** shedding-is exploited to enhance microbial virulence apparently by modulating host defences.

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13/3,AB/3 (Item 1 from file: 484)
DIALOG(R)File 484:Periodical Abs Plustext
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05060319 SUPPLIER NUMBER: 73063125
Exploitation of **syndecan-1** shedding by *Pseudomonas aeruginosa*
enhances virulence
Woo, Pyong; Pier, Gerald B; Hinkes, Michael T; Bernfield, Merton
Nature (GNAA), v411 n6833, p98-102
May 3, 2001
ISSN: 0028-0836 JOURNAL CODE: GNAA
DOCUMENT TYPE: Feature
LANGUAGE: English RECORD TYPE: Abstract

Not
proven

ABSTRACT: Cell-surface heparan sulphate proteoglycans (HSPGs) are ubiquitous and abundant receptors/co-receptors of extracellular ligands, including many microbes. Their role in microbial infections is poorly defined, however, because no cell-surface HSPG has been clearly connected to the pathogenesis of a particular microbe.

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? s syndecan
S14 6948 SYNDECAN
? s s14 and bacteria
6948 S14
2545730 BACTERIA
S15 244 S14 AND BACTERIA
? s s15 and bacterial (1w) infection
244 S15
1664494 BACTERIAL
4161151 INFECTION
95052 BACTERIAL(1W)INFECTION
S16 19 S15 AND BACTERIAL (1W) INFECTION

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>>>Duplicate detection is not supported for File 349.
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>>>No matching display code(s) found in file(s): 65, 342

17/3,AB/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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06132756 EMBASE No: 1995164395

Binding of **syndecan**-like cell surface proteoglycan receptors is required for *Neisseria gonorrhoeae* entry into human mucosal cells

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EMBO Journal (EMBO J.) (United Kingdom) 1995, 14/10 (2144-2154)

CODEN: EMJOD ISSN: 0261-4189

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Bacterial invasion of human mucosal cells is considered to be a primary event in the pathogenesis of a gonococcal infection. Here we report that cell surface heparan sulfate proteoglycans may play a role in the establishment of an infection, by functioning as receptors for the invasion-promoting gonococcal opacity protein adhesin. Chemical modification and enzymatic removal of proteoglycan receptors from cultured epithelial cells abolished opacity protein-associated gonococcal invasion, and mutant cell lines defective in proteoglycan synthesis were poor substrates for gonococcal attachment. The addition of purified receptor and receptor analogues totally blocked gonococcal entry into the cells. Heparin-affinity chromatography and receptor binding assays using recombinant **bacteria** producing defined opacity proteins and reconstituted receptor or purified receptor fragments as probes, identified one particular member of the opacity protein family (MS11-Opainf 3inf 0) as the primary ligand for this novel class of receptors for **bacteria**. Heparan sulfate proteoglycans with gonococcal binding activity were purified from various cell types derived from target tissues of gonococcal infection, including ME-180 endocervical cells and primary cultures of human corneal epithelium. The physico-chemical properties of the receptor indicate that it may belong to the **syndecan** proteoglycan family.

17/3,AB/2 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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01050815

A NOVEL RECEPTOR TREM (TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS) AND USES THEREOF

NOUVEAU RECEPTEUR TREM (RECEPTEUR DECLENCHEUR EXPRIME SUR LES CELLULES MYELOIDES) ET UTILISATIONS CORRESPONDANTES

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Patent: WO 200380667 A2 20031002 (WO 0380667)
Application: WO 2003GB1231 20030321 (PCT/WO GB0301231)
Priority Application: US 2002366525 20020322

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE
SI SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 41117

English Abstract

Novel activating receptors of the Ig super-family expressed on human myeloid cells, called TREM(s) (triggering receptor expressed on myeloid cells) are provided. Specifically, two (2) members of TREMs, TREM-4 (alpha and beta) and TREM-5 are disclosed. TREM-4 is a transmembrane glycoprotein expressed selectively in the endothelium of capillaries, in the heart and in the testis. Use of TREM-4 in treatment and diagnosis of various inflammatory diseases and heart diseases and male infertility are also provided. TREM-5 is also a transmembrane glycoprotein expressed selectively in bone marrow-derived population of leukocytes, in particular dendritic cells, and may be upregulated in certain conditions, such as cell activation, inflammation or aberrant dendritic cell function. Blockade of TREM-5 with monoclonal antibodies or soluble TREM-5-HuIgG fusion protein may reduce or block skin diseases or dendritic cell associated disorders.

French Abstract

L'invention concerne des nouveaux recepteurs d'activation de la superfamille des Ig exprimes sur les cellules myeloides humaines et designes sous le nom de TREM (recepteur declencheur exprime sur les cellules myeloides). Plus particulierement, l'invention concerne deux (2) types de TREM, soit TREM-4 (alpha et beta) et TREM-5. TREM-4 est une glycoproteine transmembranaire exprimee selectivement dans l'endothelium des capillaires, dans le coeur et dans les testicules. L'invention se rapporte en outre a l'utilisation de TREM-4 pour traiter et diagnostiquer diverses maladies inflammatoires et cardiaques ainsi que l'infertilité masculine. TREM-5 est également une proteine transmembranaire exprimee selectivement dans une population de leucocytes provenant de la moelle osseuse, et plus particulierement dans les cellules dendritiques, et peut etre regule a la hausse dans certaines conditions, notamment en cas d'activation cellulaire, d'inflammation ou d'activite aberrante des cellules dendritiques. Le blocage de TREM-5 avec des anticorps monoclonaux ou une proteine de fusion TREM-5-HuIgG permet d'attenuer ou d'inhiber des maladies de la peau ou des troubles associes aux cellules dendritiques.

01033838

MOLECULES FOR DIAGNOSTICS AND THERAPEUTICS

MOLECULES POUR LE DIAGNOSTIC ET LA THERAPEUTIQUE

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Patent: WO 200362376 A2 20030731 (WO 0362376)

Application: WO 2003US1096 20030113 (PCT/WO US0301096)

Priority Application: US 2002349384 20020116; US 2002349946 20020117; US

2002349413 20020117

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO

RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT SE SI

SK TR

(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English
Filing Language: English
Fulltext Word Count: 232005

English Abstract

The present invention provides purified human polynucleotides for diagnostics and therapeutics (dithp). Also encompassed are the polypeptides (DITHP) encoded by dithp. The invention also provides for the use of dithp, or complements, oligonucleotides, or fragments thereof in diagnostic assays. The invention further provides for vectors and host cells containing dithp for the expression of DITHP. The invention additionally provides for the use of isolated and purified DITHP to induce antibodies and to screen libraries of compounds and the use of anti-DITHP antibodies in diagnostic assays. Also provided are microarrays containing dithp and methods of use.

French Abstract

La presente invention concerne des polynucleotides humains purifies pour le diagnostic et la therapeutique (dithp). L'invention concerne egalement les polypeptides (DITHP) codes par des polynucleotides humains purifies pour le diagnostic et la therapeutique (dithp). L'invention concerne en outre l'utilisation des polynucleotides humains purifies pour le diagnostic et la therapeutique (dithp), ou des complements, des oligonucleotides, ou des fragments de ceux-ci dans des methodes diagnostiques. L'invention concerne egalement des vecteurs et de cellules hotes contenant des polynucleotides humains purifies pour le diagnostic et la therapeutique (dithp) pour l'expression des polypeptides (DITHP). L'invention concerne egalement l'utilisation des polypeptides (DITHP) isolees et purifies pour induire des anticorps et pour le criblage de bibliotheques de composees et l'utilisation d'anticorps anti-DITHP dans des methodes diagnostiques. L'invention concerne enfin des jeux ordonnes de microchantillons contenant des polynucleotides humains purifies pour le diagnostic et la therapeutique (dithp) et leurs procedes d'utilisation.

17/3,AB/4 (Item 3 from file: 349)
DIALOG(R) File 349:PCT FULLTEXT
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01019531

CELL ADHESION AND EXTRACELLULAR MATRIX PROTEINS
PROTEINES D'ADHESION CELLULAIRE ET DE MATRICE EXTRACELLULAIRE

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200347526 A2-A3 20030612 (WO 0347526)
Application: WO 2002US38437 20021126 (PCT/WO US0238437)
Priority Application: US 2001334343 20011130; US 2001340278 20011207; US
2002345069 20020104; US 2002351352 20020125; US 2002357168 20020214; US
2002369128 20020329; US 2002370802 20020405

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU
CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO
RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
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(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 127789

English Abstract

Various embodiments of the invention provide human cell adhesion and
extracellular matrix proteins (CADECM) and polynucleotides which identify
and encode CADECM. Embodiments of the invention also provide expression

vectors, host cells, antibodies, agonists, and antagonists. Other embodiments provide methods for diagnosing, treating, or preventing disorders associated with aberrant expression of CADECM.

French Abstract

Dans differents modes de realisation, l'invention concerne des proteines humaines d'adhesion cellulaire et de matrice extracellulaire (CADECM) ainsi que des polynucleotides identifiant et codant ces CADECM. L'invention concerne egalement des vecteurs d'expression, des cellules hotes, des anticorps, des agonistes et des antagonistes. Cette invention se rapporte en outre a des procedes de diagnostic, de traitement, ou de prevention de troubles associes a une expression aberrante des CADECM.

17/3,AB/5 (Item 4 from file: 349)
DIALOG(R) File 349:PCT FULLTEXT
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00964355

MOLECULES FOR DIAGNOSTICS AND THERAPEUTICS

MOLECULES UTILISEES A DES FINS DIAGNOSTIQUES ET THERAPEUTIQUES

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Set	Items	Description
S1	7546	SYNDECAN
S2	2359563	S1 AND BACTERIA OR BACTERIAL
S3	550	S2 AND S1
S4	29	S3 AND GENISTEIN
S5	27	RD (unique items)
? s s3 and tyrphostin (1w) a47		
	550	S3
	9114	TYRPHOSTIN
	3480	A47
	228	TYRPHOSTIN(1W)A47
S6	1	S3 AND TYRPHOSTIN (1W) A47